

Amendments to the Specification:

**Please replace paragraph [0046], beginning at line 28 on page 14 of the instant specification, with the following amended paragraph:**

[0046] By analogy to known kinase structures, the  $\gamma$ -phosphate of ATP would occupy an area around the sidechains of residues D964 (N964 in the catalytically inactive mutant, (SEQ ID NO 2). The sidechain of R968 also contributes to this region. The predominant available interaction type was hydrogen bonding, with quite complex coordination possible.

**Please replace paragraph [0079], beginning at line 3 on page 23 of the instant specification, with the following amended paragraph:**

[0079] The comparison of sequences and determination of percent identity and homology between two sequences can be accomplished using a mathematical algorithm. (*Computational Molecular Biology*, Lesk, A.M., ed., Oxford University Press, New York, 1988; *Biocomputing: Informatics and Genome Projects*, Smith, D.W., ed., Academic Press, New York, 1993; *Computer Analysis of Sequence Data, Part 1*, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; *Sequence Analysis in Molecular Biology*, von Heinje, G., Academic Press, 1987; and *Sequence Analysis Primer*, Gribskov, M. and Devereaux, J. eds., M. Stockton Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (~~available on March 29, 2000 at <http://www.gcg.com>~~), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of, for example, 16, 14, 12, 10, 8, 6, or 4 and a length weight of, for example, 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (Devereaux, J., et al., *Nucleic Acids Res.* 12(1):387 (1984)) (~~available on March 29, 2000 at <http://www.gcg.com>~~), using a NWSgapdna.CMP matrix and a gap weight of, for example, 40, 50, 60, 70, or 80 and a length weight of, for example, 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is

determined using the algorithm of E. Meyers and W. Miller (*CABIOS*, 4:11-17 (1989)) which has been incorporated into the ALIGN program (version 2.0), using, for example, a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

**Please replace paragraph [0080], beginning at page 23, line 26 of the instant specification, with the following amended paragraph:**

[0080] The protein sequences of the present invention, for example, amino acids 802-1124 of human Tie-2 (SEQ ID NO 1), can further be used as a "query sequence" to perform a search against databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (*J. Mol. Biol.* 215:403-10 (1990)). BLAST protein searches can be performed with the XBLAST program, for example, score = 50, word length = 3, to obtain amino acid sequences homologous to the proteins of the invention. To obtain gapped alignments for comparison purposes, gapped BLAST can be utilized as described in Altschul *et al.*, (*Nucleic Acids Res.* 25(17):3389-3402 (1997)). When utilizing BLAST and gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST ) can be used as given on March 29, 2000 at <http://www.ncbi.nlm.nih.gov>.

**Please replace paragraph [0081], beginning at page 24, line 9 of the instant specification, with the following amended paragraph:**

[0081] Homology for amino acid sequences can be defined in terms of the parameters set by the Advanced Blast search available from NCBI (the National Center for Biotechnology Information; ~~see, for Advanced BLAST, [www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast?Jform=1](http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast?Jform=1) (on March 29, 2000))~~). These default parameters, recommended for a query molecule of length greater than 85 amino acid residues or nucleotides have been set as follows: gap existence cost, 11, per residue gap cost, 1; lambda ratio, 0.85. Further explanation of version

2.0 of BLAST can be found ~~on related website pages and~~ in Altschul, S.F. *et al.*, *Nucleic Acids Res.* 25:3389-3402 (1997).